Economically Important Production Diseases of Dairy Animals

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The production diseases of the dairy cow are a manifestation of the cow's inability to cope with the metabolic demands of high production, and they continue to be a cause of economic loss to the dairy industry and an animal welfare concern (Mulligan and Doherty, 2008). According to Radostits *et al.* (2000) the production diseases comprised of diseases associated with an imbalances between the rate of input of essential dietary nutrients and the output of the production such as milk fever, ketosis, hypomagnesemia and mastitis etc.

Milk is the major source of income generated on dairy farms, and over the past several decades, milk production by dairy cows has increased markedly. However, this improvement comes at the cost of higher incidences of reproductive health problems and reduced fertility. The livestock sector plays a vital role in the economies of many developing countries including India. It provides food, or more specifically animal protein in human diets, income, employment and possibly foreign exchange. For low income producers, livestock also serve as a store of wealth; provide draught power and organic fertilizers for crop production and a means of transport. India, one of the world`s largest and fastest growing markets for milk and milk products is getting almost 7.5 growth annually in value terms for milk and milk products. The growth in the market size includes the organised and unorganised sector, which is of US $ 47.6 billion (INR 2,000 billion). The demand for value added milk products, such as cheese, dahi (Indian yoghurt) and probiotic drinks is increasing at a double digit rate in India. Currently, India seems to be self-sufficient in meeting the requirement for milk and milk products. But as the demand is growing faster than supply, there could be serious issues with respect to self-sufficiency in the near future. India's annual milk production has more than trebled in the last 40 years, rising from 21 million tonnes in 1968 to an anticipated 108 million tonnes in 2008-2009. In 2006-07, Indian milk production, which includes cow and buffalo milk, stood at 100.9 million tones and accounted for approximately 15 per cent of total world milk production (Commodityonline, 2008). India is expected to maintain last year's record of being the world's largest milk producer, with an estimated 110 million tonnes in 2008-09. The country achieved the distinction with the production of 104.8 million tonnes in the 2007-08, according to a spokesman of the National Dairy Development Board (The Hindu, 18/12/09). In the Indian context of poverty and malnutrition, milk has a special role to play for its many nutritional advantages as well as providing supplementary income to some 70 million farmers in over 500,000 remote villages. Any increase in milk production is dependent on the farm gate price received by the producer. In the last three years, farm gate prices have increased by more than 50 percent. Focused efforts would be required on two front such as increasing farm size (currently the average number of animals per producer is three to four), and increasing productivity of milk producing animals. High producing dairy cows need to mobilize body reserves to be able to sustain their milk production. In early lactation, until energy intake assures the requirements, dairy cows, especially high producing breeds, enter a state of negative energy balance (NEB), losing high amounts of body condition. Presently researchers and farmers are focusing towards cross breeding practices to produce high yielding dairy animals according to demand of milk and milk products. But along these practices farmers are not much aware vis-à-vis nutrient and energy supply to animals according to their production and results increase the susceptibility to production diseases, ultimately decrease in the milk production. In recent years, scarcity of animal feed and forage in some part of the country (e.g. Vidharbh region of Maharashtra state) has drastically influenced the production through production disease in dairy animals. Here, interesting findings are that between 1995 to 2000, daily milk yields have increased at faster rate of local cattle (+34 percent) and buffaloes (+17 percent) than for cross bred cows, whose daily yields declined by 5% in the same period. From 1995 to 2001, the number of local has remained constant while the number of buffaloes and cross bred cows have increased by 10% and 50% respectively, these data justify the emphasis on cross breeding programme.

The production diseases are defined as *"a number of metabolic disorders of increasing importance in agriculture"*. Over the years, this definition has expanded to include not only metabolic and nutritional diseases, but also many diseases of an infectious and genetic nature. Payne's definition of production disease as a **"man-made problem"** consisting of *"a breakdown of the various metabolic systems of the body under the combined strain of high production and modern intensive husbandry"* (Payne, 1972) likely still holds the key to understanding and preventing production diseases.

A major challenge for dairy producers and Veterinarians is to maintain a dairy cow health during the transition/periparturient period. The periparturient period of dairy cows refers to the time frame near parturition. The transition period for dairy cows is generally defined as the time period from 3 weeks prior to parturition through 3 weeks after parturition (Smith, 2005). It is a pivotal time in the production cycle of the cow, in which cattle are at high risk for the occurrence of most of production diseases. Fetal dry weight increases exponentially during gestation, particularly during last trimester of pregnancy, hence during this period higher demand for energy, protein, calcium and other nutrients to fulfill the requirement. It is now recognized that defining and meeting the nutritional requirements of the transition dairy cow can greatly impact animal health, production in the ensuing lactation, overall longevity, and animal well-being. The transition to lactation underscores the importance of gluconeogenesis in ruminants as hypoglycemia, ketosis, and related metabolic disorders are often observed when gluconeogenic capacity fails to adapt to the increased demands for glucose to support lactose synthesis and mammary metabolism. Ketosis is accompanied by fatty liver and

cows that develop fatty liver and ketosis have reduced feed intake, lower gluconeogenic capacity, lower milk production, and an increased risk for developing other metabolic and infectious diseases (Curtis *et al.*, 1985). During the transition period, the immunologic status of the cow is compromised. Neutrophil and lymphocyte function is depressed and plasma concentrations of other components of the immune system are decreased (Goff and Horst, 1997). It is not known why immune function is suppressed but it may be related to the nutritional and physiologic status of the cow. Estrogen and glucocorticoids are immunosuppressive agents and they increase in plasma as parturition approaches (Goff and Horst, 1997). Intake of vitamin A and E and other nutrients essential for immune function may be decreased as DMI is reduced during the periparturient period.

Inadequate nutrients provided to the transition cow can result in increased costs for veterinary treatment and loss of production potential. Problems during the transition period often result in the loss of 10 to 20 lbs. of peak milk, which translates into economic losses up to $600 for that lactation. To maximize productivity and ensure successful reproduction, rations fed during this time need to be nutrient dense and allow for proper transitioning of the diet to the lactating cow ration.

Metabolic disease incidence typically increases as milk production increases and as herds become larger. In general, subclinical disease incidence is more common than clinical mastitis. Frequently it goes unnoticed and is associated with significant economic losses that include increased clinical diseases risks, impaired milk production and reduced reproductive performance, and culling losses.

The present paper is focused on the important production disease like milk fever, ketosis and mastitis, those directly or indirectly economically important to dairy farmers and affects the health and welfare of dairy animals.

DOES HIGH MILK YIELD CAUSE PRODUCTION DISEASE?

When addressing this question, one must remember that "milk yield" is not the only risk factor for "disease." The occurrence of disease must also be viewed in relation to husbandry and management conditions. It is noteworthy that Payne's 1972 indictment of production disease as a "***man-made problem"*** did not implicate "strain of high milk production" as a primary cause of production disease, but only one component of a two-way interaction. Nevertheless, the push to attain high milk yield has been a common evil invoked by many to explain production diseases over the subsequent three decades. In general, however, the scientific literature describing the epidemiological relationships between high milk yield and increased production disease is inconclusive at best. Sharma (2003) had been reported that high yielders cows are more susceptible to mastitis as compared to low milk producer. Despite the fact that available data were inconclusive, Ingvartsen *et al.* (2003) concluded that continued selection for milk yield *"will continue to increase lactational incidence rates"* for ketosis and lameness. Dufflied (2006) reported that higher producing cows are more likely to be hyperketonemic, a larger proportion of subclinically ketotic cows combined with misclassification bias of clinical ketosis cases could mute any association between clinical ketosis and previous lactation milk yield. Studies comparing health data between lines of dairy cows selected for high milk yield and control lines maintained at average milk yield generally show higher health care costs for the high yielding cows (Dunklee *et al.*, 1994; Jones *et al.*, 1994). Hansen (2000) argued that selection for body traits, especially those related to udder conformation, body size, and angularity, may be placing cows at greater risk for production disease. For example, placing favorable emphasis on cows that appear sharper might result in cows that are more prone to metabolic problems such as ketosis and displaced abomasum.

Dry matter intake, and subsequently nutrient intake, is reduced greatly a few days before calving and remains low for a few days after calving. At the same time, requirements for nutrients are increased because of colostrum synthesis and events associated with parturition. During this period, cows are usually in severe negative energy balance and serum or plasma concentrations of several minerals and vitamins are reduced, suggesting lowered status (Goff, 2006). This period often represents a time when the immune system of the cow is severely suppressed, making cows particularly vulnerable to production and infectious diseases such as milk fever, ketosis, mastitis etc. Negative energy balance initiates the mobilization of body lipids, which are released as non-esterified fatty acids (NEFA) from adipose tissue. Increased NEFA levels are temporally associated with periparturient immune function suppression and may contribute to impairment of the immune system in dairy cows (Rukkwamsuk *et al.*, 1999). Furthermore, elevated levels of β-hydroxybutyric acid (BHBA) and other ketones have been shown to impair important functions of immune cells with possible implications for systemic infections postpartum (Klucinski *et al.*, 1988). Kremer *et al.* (1993) reported that cows in negative energy balance (with elevated BHBA) prior to experimental infection of the mammary gland experienced more severe mastitis compared to cows with low blood BHBA concentrations, indicating that negative energy balance may predispose cows to severe infections. Hoeben *et al.* (1997) reported that exposure of PMN to elevated levels of BHBA reduced PMN respiratory burst and they concluded that BHBA may, in part, be responsible for the higher susceptibility to local and systemic infections during the postpartum period.

On the other hand, selection for high milk yield must also concurrently increase the ability of support systems (*e.g.*, gastrointestinal tract, liver, adipose tissue, skeletal muscle) to provide and process nutrients for the mammary gland to manufacture high milk yield. This principle is embodied in the concepts of "homeorhesis" as described by Bauman and Currie (1980), in which needs for the developing late-term fetus or copious milk secretion in early lactation assume top priority for available nutrients. As pointed out by Ingvartsen *et al.* (2003), the greatest incidence of production diseases is very early after calving and occurs concurrently with the greatest rate of increase (acceleration) of daily milk yield, not with peak milk yield itself. The rate of acceleration of milk yield is greater for higher yielding cows than lower yielding cows. Peak disease incidence also coincides with the nadir in energy balance and the greatest rate of body fat mobilization, as reflected in peak non-esterified fatty acids (NEFA) concentrations in blood. Thus, the conceptual view that high-producing cows are more susceptible to environmental insults that in turn disturb homeostasis and cause production disease is more attractive than the notion that production disease is caused by high production *per se*. The relationship between high milk yield and immune system has also been established and found that in high yielders, immune system is suppressed due to many cofactors.

The onset of milk production imposes tremendous challenges to the mechanisms responsible for energy, protein, and mineral homeostasis in the cow. Negative energy, protein, and/or mineral balance associated with the onset of lactation may be partially responsible for the immunosuppression observed in periparturient dairy cattle. Neutrophil and lymphocyte function is diminished in the periparturient period, especially in the dairy cow. Some reports suggest that there are major factors responsible for suppressed immune system in high yielder like- 1) the mammary gland may produce substances which directly affect immune cell populations, or 2) metabolic demands associated with the onset of lactation negatively impact the composition of circulating immune cells populations.

The mechanisms responsible for PMN function impairment in periparturient dairy cows are poorly understood. The metabolic challenges associate with late gestation and the onset of lactation could be responsible in part for PMN function impairment during this time (Kimura *et al.*, 1999).

COMPTON METABOLIC PROFILE TEST (CMPT)

A "metabolic profile" is defined as a series of specific analytical tests run in combination and used as a diagnostic aid (Ingraham and Kappel, 1988). Although similar samples and analytical methods are used in assessing disease diagnosis or metabolic profiling, their approaches to sampling and interpretation are different (Herdt *et al.*, 2001). The use of blood metabolites is not new concept. It started in 1950 (Rowlands, 1980). In the sixties, automated analytical equipment was developed, making the analysis of blood metabolites a routine technique used to assess the metabolic status of an animal. Metabolic profiling has its roots in Compton, England in the 1970's. It was first established by Payne *et al.* (1970) as a tool for assessing metabolic status and helping in the diagnosis of metabolic/production disorders in dairy herds. Subsequently, many researchers have applied CMPT to improve feeding management (Amano *et al.*, 1992; Blowey, 1975), detect subclinical health problems and prevent production diseases. CMPT, in conjunction with animal and facility evaluation, body condition scoring and ration evaluation, is an important useful tool for nutritional evaluation in dairy herds (Van Saun, 1997). In 1978 Payne put together a group of metabolites into a single package called the ***"Compton Metabolic Profile Test"***. The development of the "Compton Metabolic Profile Test" coincided with an increased intensification of livestock production and with a greater effort being made by the farmer to produce maximum output with maximum costs. This increased output puts strain on the metabolism of the animal, which leads to increased risk of metabolic imbalances. The "Compton Metabolic Profile Test" was designed to monitor the metabolic health of cows in dairy herd in relation to management, nutrition, milk production, disease and to aid in the diagnosis of metabolic disorders. It does this by comparing the average concentration of blood constituents of a group of cows to the defined mean concentration values (Table 1). There are two main objectives for conducting serum metabolite testing in periparturient cows. Although these objectives may overlap, it is worth stating them for clarity.

1. Cow-level interpretation – There is a problem with this cow and treatment and/or further examination may be warranted.

2. Herd-level interpretation - There is a potential problem with the current herd management that needs to be investigated.

Cow and herd level interpretation can be conducted with the same samples but they differ in that we are differentiating between an individual or group problem.

Table 1. Reference values of blood constituents.

Blood constituent	Reference value	Remark
Hb	12-14 g/dl	Uncoagulated blood with EDTA
PCV	36-42%	Uncoagulated blood with EDTA
Glucose	46-80 mg/dl	Serum is the sample of choice.
BHB	10-12 mg/dl	- Serum is the sample of choice. - Concentrations greater than 10-12 mg/dl are consistent with subclinical ketosis. - Serum is the blood sample of choice. - Values are highest 2-4 hours post feeding.
NEFA	Dry cows (3 weeks to 3 days before calving)- <0.3 mEq/L Fresh cows (>3 days in milk)- <0.7 mEq/L	- Values are stable in frozen plasma sample.
Total protein		
Albumin	≥3 g/dl	- Serum is the sample of choice. - Concentrations normally declines near parturition, so reference values based on cattle at other times are too high. Values <2.5 g/dl are consistent with inadequate protein stores.
Blood urea nitrogen (BUN)	13-16 mg/dl	- Serum is the sample of choice.
Aspartate aminotransferase	<100 IU/L	- Serum is the blood sample of choice. Activity is relatively stable in serum.
Blood selenium	For individual adults- 120-250	- Uncoagulated blood with EDTA.

	ng/ml. For herd mean- 185 ng/ml (ppb).	- Good indicator of nutritional adequacy.
Copper	For individual adults- 0.6-1.0 mg/L (ppm). For herd mean- 0.8 mg/L (ppm).	- Serum is the sample of choice.
Zinc	For individual adults- 0.8-1.4 mg/L (ppm). For herd mean- 1.1 mg/L (ppm).	- Serum is the sample of choice.
Iron	39-155 μg/dl	- Serum is the sample of choice.
Ca	For individual adults- 8.5-11 mg/dl. For herd mean- 9.5 mg/dl.	- Serum is the sample of choice.
P	5.6-6.5 mg/dl	- Serum is the sample of choice.
Na	132-152 mEq/L	- Serum is the sample of choice.
K	3.9-5.8 mEq/L	- Serum is the sample of choice.
Mg	1.8-2.4 mg/dl	- Serum is the sample of choice.

Collection and analysis of blood samples-

Blood can be collected directly from jugular vein in a suitable anticoagulant. Sample collection and handling are important if one is to expect useful diagnostic information. Samples should be taken with feeding management in mind. Several metabolites are influenced by feeding and have significant diurnal variation (Hoff and Duffield, 2009) (Table 1). It is important therefore to sample animals on individual farms at approximately the same time of day. Measures should be taken to prevent hemolysis. The serum should be spun and separated within 2-3 hours and refrigerated. Other pertinent information for interpretation should be included. Type of blood sample e.g. plasma or serum, also affect the values of blood constituents. A study was conducted by Okada and Yasuda (2001) and found that FFA, BHB, total cholesterol, phospholipids and AST were lower in plasma, while total protein and albumin were higher in plasma. Regarding glucose level there was no difference between serum and heparinated plasma. When separated serum was refrigerated or frozen glucose, total cholesterol, BHB, total protein, albumin, BUN and inorganic phosphorus were stable for 7 days, while FFA and AST were relatively unstable.

Blood sample should be collected from different stages of lactation and dry (Table 2). Testing is broad based and includes analytes reflecting energy balance (Glucose, NEFA, BHBA), protein status (total protein, albumin, urea nitrogen), liver function (alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (AP), cholesterol, and triglycerides) and macromineral (sodium, potassium, calcium, magnesium) homeostasis. This can also be expanded to include microminerals (copper, zinc, iron) and vitamins.

Table 2. Suggested physiologic groupings for collecting blood samples in completing metabolic profile testing using individual or pooled samples.

Physiological group	Time relative to calving/definition
Far off dry	>10 days following dry off and <30 prior to calving
Close-up Dry	Between 3 and 21 days prior to calving (3 to 14 days best)
Fresh	3 to 30 days in milk (7 to 21 days best)
Lactation groups	Define as needed based on disease conditions, production level or other problem.

Source: Van Saun (2007)

Interpretation –

The interpretation of data in CMPT is most important aspect to diagnose a specific problem at herd or individual level. Here interpretation is given as per Hoff and Duffield (2009).

Energy status:

Blood glucose is an insensitive measure of energy status because it is subject to tight homeostatic regulation.

Non-esterified fatty acids (NEFA) are the blood metabolites most directly associated with energy balance. NEFA is most valuable in the late (close-up) dry period, particularly within a week of calving. NEFA reflects the magnitude of mobilization of fat from storage. BHBA indicates the completeness of oxidization ("burning") of fat in the liver.

Beta-hydroxybutyrate (BHB) is the ketone body of choice for routine measurement because of its stability in serum or plasma. Blood ketone bodies are elevated in association with poor carbohydrate status only when concurrently associated with negative energy balance. BHBA is most useful within the first month post-calving, particularly in the first 2 weeks postpartum

Protein status:

Blood urea levels can be used as an indirect measure of rumen ammonia in ruminants with normal kidney function. Although no specific disease state is associated with abnormal herd urea levels, valuable information concerning dietary protein content and utilization can be detected from herd urea levels – high blood urea levels are consistent with excessive protein intake.

Mineral and vitamin status:

Most nutrients are homeostatically regulated, therefore their value in profile testing for monitoring and assessment of nutritional status is limited. However, sampling cows when they are metabolically stressed, e.g., just prior to and following calving, could potentially result in identifying cows that are more prone to metabolic disease problems. Liver trace minerals are better indicators of dietary adequacy, but serum levels may be of value in chronic dietary problems. Fat-soluble vitamins can be easily assessed in serum or liver samples. Gestational micro-mineral and vitamin losses may significantly affect the cow's reserves and thus her metabolic function. Mineral and vitamin supplementation may have been reduced during the dry period. Deficiencies in micro-minerals, such as copper, manganese, zinc and selenium, as well as fat-soluble vitamins, may lead to a compromised immune system.

A **trace element screen** (Ca, Cu, Fe, Mg, Zn), as well as selenium and vitamin E, can be added to the CMPT, as needed.

Oetzel has advocated that evaluating a proportion of individual samples relative to a given reference criteria may be of greater value in assessing disease risk (Oetzel, 2004). Analytes with a threshold value above or below which is associated with disease risk are best evaluated as a proportion rather than a mean. For example, one could determine rumen pH to diagnose subacute ruminal acidosis (SARA) in a herd. Elevated prefresh NEFA concentration (≥ 0.4 mmol/L) and postfresh BHB concentration (≥1200-1400 µmol/L) are recognized risk factors for ketosis and left displaced abomasum (Duffield, 2004; LeBlanc, 2006). Low blood calcium concentration (< 2.0 mmol/L), immediately postcalving, is a risk indicator for subclinical hypocalcemia (Oetzel, 2004). Blood urea nitrogen (BUN) and urine pH have also been advocated as potential indicators for assessing herd protein status and anionic salt responsiveness, respectively (Oetzel, 2004).

MILK FEVER

Milk fever is an important production disease occurring most commonly in adult cows within 48-72 hours after parturition, which is characterized clinically by hypocalcemia, general muscular weakness, circulatory collapse and depression of consciousness (Radostits *et al.*, 2000). The name milk fever is misleading since the cow does not have a fever. This disease has been known by a number of terms including parturient paresis, milk fever, parturient apoplexy, eclampsia, and paresis peurperalis. The term "parturient hypocalcemia" (PH) is to refer to the classic clinical syndrome. When milk fever is results due to imbalance in blood Ca, P and Mg levels, known as "Milk fever complex) (Sharma *et al.*, 2005). Generally the milk fever is sporadic but on individual farms the incidence may rarely reach 25 to 30% of susceptible cows. The incidence of milk fever is higher in dairy cows than beef cows and increases with age and yield. Milk fever undoubtedly increased in incidence during the 1970s and 1980s when levels of around 9 per cent per annum were being reported. Goff (2006) recently reported that incidence of milk fever in US was 5.9% in 1995 and 5.2% in 2001. The incidence of milk fever in organic cows has been reported as being low (Weller and Cooper, 1996). One of the main reasons for this may be the generally lower milk yield on organic dairy farms (Pryce *et al.*, 1999). The disease does appear to be more common when dry cows are fed grass rather than conserved fodder. Milk fever is a common cause of death and is probably the most common cause of apparent sudden death in dairy cows. It is also a common cause of dystokia and hence stillborn calves. Hypocalcemia or low blood Ca (not just milk fever) impairs abomasum contraction leading to more metabolic disorders. Hypocalcemia cause secretion of cortisol which impairs the immune system of the fresh cow (Fig. 1) (Wang *et al.*, 1991). Cows developing milk fever have higher plasma cortisol concentrations than do non-milk fever cows (Goff *et al.*, 1989). Muscle tone decreases in most body systems, particularly in the cardiovascular, reproductive, and digestive systems, and possibly in the mammary system. Blood flow to the extremities is reduced, causing the characteristic cold ears of a cow suffering from milk fever. Jonsson and Daniel (1997) found that there was also a significant reduction in blood flow to the ovaries of sheep with induced hypocalcemia. This would result in suppressed ovarian function, including progesterone synthesis and follicular development. Unfortunately, the highest incidence of hypocalcemia is during the first 6 weeks after calving, a critical time for resumption of ovarian activity. Milk fever cows also exhibit a greater decline in feed intake (Fig. 1) after calving than non-milk fever cows (Goff and Horst, 1997), exacerbating the negative energy balance commonly observed in early lactation. In addition, hypocalcemia prevents secretion of insulin (Littledike *et al.*, 1970), preventing tissue uptake of glucose which would exacerbate lipid mobilization at calving, increasing the risk of ketosis.

to be contd….

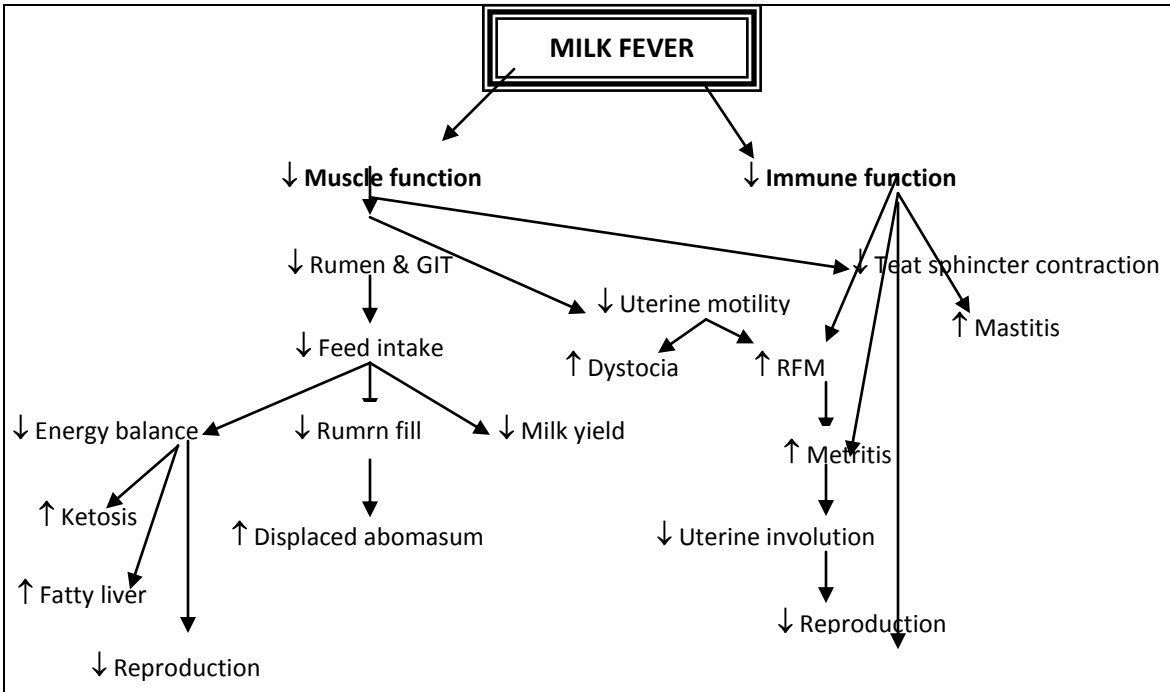

Fig. 1. Consequences of milk fever [Adopted from Mulligan *et al.* (2006)].

Importance

Rajala-Schultz *et al.* (1999) found that milk fever alone caused a milk loss of between 1.1 and 2.9 kg/d during the first 4 to 6 weeks following parturition. It can also reduce the productive life of the cow by as much as 3.4 years. The average cost per case of milk fever has been estimated at $334, based on direct treatment cost and estimated production losses (Horst *et al.*, 1997). Milk fever also increases the risk of other production diseases, primarily because it has a detrimental affect on smooth muscle function. The cost of milk fever in Sweden was estimated in 1969 to be at least 10 million Swedish crowns annually (Jonsson, 1960). Payne, in 1966, listed the national estimate of depreciation due to milk fever in Great Britain at 161,000 pounds annually (Pyne, 1966). The annual loss from milk fever in the United States was estimated to be approximately $10.5 million in 1965 (Littledike, 1974). In France, 150,000 cases of milk fever were reported in 1959, and a 10-million franc loss was estimated (Lavor *et al.*, 1961). Losses from this disease are difficult to quantitate because of the many indirect costs e.g. losses due to culling of cows, decreased milk production, treatment cost, feed costs and other extra supplementation of minerals. By any measure, milk fever costs the dairy industry many millions of dollars each year and, therefore, is of considerable economic significance (Littledike *et al.*, 1981).

Predisposing factors

There are several important predisposing factors that influence the occurrence of milk fever and these accounts for the wide variation of incidence.

1. *Breed*- Several investigators(Erb and Martin, 1978; Kusumanti *et al.*, 1993) have been suggested that the Jersey and, to lesser extent, the Swedish Red and White and Norwegian Red breeds have a higher incidence of milk fever as opposed to Holstein cows. The exact reasons for this increased susceptibility are unclear. Recently, Goff *et al.* (1995) have suggests that intestine of Jersey cows possesses 15% fewer receptors for $1,25(OH)_2D_3$ than the intestine of Holstein cows. Lower receptors would result in a loss of target tissue sensitivity to $1,25(OH)_2D_3$. At parturition, plasma $1,25(OH)_2D_3$ is elevated as the cow becomes hypocalcemic. Normally, the elevated $1,25(OH)_2D_3$ would result in enhanced bone Ca resorption and intestinal Ca absorption. However, with a reduced number of $1,25(OH)_2D_3$ receptors, the activation of genomic events by $1,25(OH)_2D_3$ is less efficient, resulting in increased susceptibility to milk fever. This would indicate a genetic predilection for this disease and is probably related to the relatively high production level for a small breed.

2. *Age*- The risk of a cow developing milk fever increases with age. It is rare for milk fever to occur at the first calving and relatively uncommon at the second. The incidence does appear to increase with age and incidence levels of 20 per cent or more are common at the sixth calving and beyond. More importantly, the bones of heifers are still growing. Growing bones have large numbers of osteoclasts present, which can respond to parathyroid hormone more readily than the bones of mature cows. Lower number of active osteoblasts in older cows means fewer cells to respond to PTH and mobilize bone Ca. Advancing age results in increased milk production, resulting in a higher demand for Ca. Aging also results in a decline in the ability to mobilize Ca from bone stores and a decline in the active transport of Ca in the intestine, as well as impaired production of $1,25(OH)_2D_3$. Horst *et al.* (1990) recently demonstrated that intestinal receptors for $1,25(OH)_2D_3$ decline as age advances.

3. *Nutrition*- Metabolic alkalosis predisposes cows to milk fever and subclinical hypocalcemia. Metabolic alkalosis blunts the response of the cow to parathyroid hormone (PTH) (Goff *et al.* 1991). In vitro studies suggest the conformation

of the PTH receptor is altered during metabolic alkalosis rendering the tissues less sensitive to PTH. Lack of PTH responsiveness by bone tissue prevents effective utilization of bone canaliculi fluid Ca, sometimes referred to as osteocytic osteolysis, and prevents activation of osteoclastic bone resorption. Failure of the kidneys to respond to PTH reduces renal reabsorption of Ca from the glomerular filtrate. More importantly, the kidneys fail to convert 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D. Therefore enhanced intestinal absorption of dietary Ca that normally would help restore blood Ca to normal, fails to be instituted. Metabolic alkalosis is largely the result of a diet that supplies more cations (K, sodium (Na), Ca, and Mg) than anions (chloride (Cl), sulfate (SO4), and phosphate (PO4)) to the blood.

Manipulation of dietary Ca and P is known to have dramatic effects on the incidence of milk fever. The feeding of diets high in Ca during the prepartum period can result in a high incidence of milk fever. With a Ca:P ratio of 6:1, 30% cows developed milk fever, at a Ca:P ratio of 1:1, 15% developed the disease, and at a ratio of 1:3.3 no cases occurred.

In the vitamin D deficiency, reduction in the production of $1,25(OH)_2D_3$, resulting increase the risk for milk fever. Horst *et al.*, (1994) have determined the plasma $1,25(OH)_2D_3$ concentration below 5ng/ml are indicating of vitamin D deficiency and concentrations of 200-300ng/ml would indicate vitamin D toxicosis. Normal cows have plasma $25(OH)_2D_3$ concentrations between 20 and 50ng/ml.

Etiology

The onset of lactation places such a large demand on the calcium homeostatic mechanisms of the body that most cows develop some degree of hypocalcemia at calving. In some cases, plasma calcium concentrations become too low to support nerve and muscle function, resulting in parturient paresis or milk fever. Milk fever occurs when calcium leaves the blood to support milk production faster than Ca can be put back into the blood from the diet, skeletal Ca stores, and renal conservation of calcium. The onset of lactation places such a large demand on the calcium homeostatic mechanisms of the body that most cows develop some degree of hypocalcemia at calving (Goff, *et al.*, 1987; Horst *et al.*, 1994). The entire extracellular pool will have only 8 to 9g Ca. In some cases, plasma calcium concentrations become too low to support nerve and muscle function, resulting in parturient paresis or milk fever. A cow producing 10 kg of colostrum (2.3g of Ca/kg) will loss 23g of Ca in a single milking. This is about 9 times as much Ca as that present in the entire plasma Ca pool of the cow. Normally extracellular Ca concentration is around 10,000 greater than intracellular resting Ca concentration. A 50% decline in extracellular ionosed Ca concentration, typical of the cow with milk fever. This hypocalcemia is caused by an imbalance between Ca output in the colostrum and influx of Ca to the extracellular pool from intestine and bone.

In order to prevent blood calcium from decreasing, the cow must replace calcium lost to milk by withdrawing calcium from bone or by increasing the efficient absorption of dietary calcium. Plasma Ca concentration is under the control of parathyroid hormone, calcitonin, and the metabolites of vitamin D (Goff *et al.*, 1995). Bone calcium mobilization is regulated by parathyroid hormone (PTH) produced by the parathyroid glands. Whenever there is a drop in blood calcium, blood PTH levels increase dramatically. Renal tubular reabsorption of Ca is also enhanced by PTH. However, the total amount of Ca that can be recovered by reducing urinary Ca excretion is relatively small.

A second hormone, 1,25-dihydroxyvitamin D, is required to stimulate the intestine to efficiently absorb dietary calcium. This hormone is made within the kidney from vitamin D in response to an increase in blood PTH (Goff, 2006). Milk fever occurs when cattle do not remove enough Ca from their bones and the diet to replace Ca lost to milk. This occurs because a key hormone involved in Ca metabolism, parathyroid hormone, acts only poorly on bone or kidney tissues when the blood pH is high (Goff and Horst, 1997). Blood pH of cattle is often alkaline because forage K is often excessively high.

Oestrogens also inhibit calcium mobilization and as oestrogen levels rise at parturition this will have a negative effect on the adaptation process to maintain calcium levels. Milk fever does occasionally occur during lactation, usually in association with oestrus. This again would be due to the inhibitory effect of oestrogens.

In conclusion, milk fever is caused due to disturbance in Ca homeostasis. Calcium homeostatic mechanism is influenced by mainly 3 factors- a) excessive loss of Ca++ in the colostrums beyond the capacity of absorption from intestine, b) impairment of absorption of Ca++ from intestine at parturition, and c) mobilization of Ca++ from storage in skeleton may not be sufficiently rapid to maintain normal serum level (Sharma *et al.*, 2006).

Clinical signs

The main clinical manifestations are divided into three stages.

First stage or Stage of excitement:

- Anorexia (decreased appetite)
- Nervousness or hypersensitivity
- Mixed excitement or tetany without recumbency
- Weakness or weight shifting
- Stiffness of hind legs
- Rapid heart rate
- Rectal temperature is usually normal or above normal (>39°C).

Second stage or Stage of sternal recumbency:

- Sternal recumbency comprising down on chest and drowsiness
- Characteristic "S" shaped posture- sitting with lateral kink in neck or head turned to lateral flank.
- Depression
- Fine muscle tremors

- Rapid heart rate with decreased intensity of heart sounds
- Cold extremities
- Decreased rectal temperature (35.6 to 37.8°C)
- Decreased gastrointestinal activity
- Pupils dilated and unresponsive to light

Third stage or Stage of lateral recumbency:

- Lateral recumbency, comprising of almost comatose condition, progressing to loss of consciousness
- Severe bloat
- Flaccid muscles
- Profound gastrointestinal atony
- Rapid heart rate
- Impalpable pulse and almost inaudible heart sounds.

Diagnosis

1. History taking
   - Occurs in mature cows usually 5-9 years old, within 72 hours after parturition.
   - Occurs in highest milk producing period.
   - Higher incidence in the Jersey breed.
2. Clinical examination

Under this though examine the animal after collecting the detail history. Clinical signs include early excitement and tetany, hypothermia, flaccidity pupil dilation, impalpable pulse, no rumen movement, soft heart sounds, fast heartbeats are fast (80-100 per minutes), decreased reflex, depression coma, bloated and death.

3. Laboratory diagnosis

Hypocalcemia- Milk fever can be defined as low blood total calcium (8.0 mg/dl) or low blood ionized calcium (4.0 mg/dl), with or without clinical signs of hypocalcemia. The major change in the blood of cows with milk fever is blood calcium. Normal level in a dairy cow is 8-10 mg/dl. The level drops to 8 mg/dl at calving. In milk fever cows, blood calcium level drops to 6.5, 5.5, and 4.5 mg/dl in stage I, II, and III, respectively. The drop in blood calcium level is usually accompanied by a drop in blood P and increase in blood K and Mg levels. Direct determination of blood calcium is the more accurate method to diagnose a case of milk fever.

Blood calcium levels in healthy and milk fever cows-

Normal Lactating cow	- 8.4-10.2 mg/dl
Normal at calving	- 6.8-8.6 mg/dl
Slight milk fever	- 4.9-7.5 mg/dl
Moderate milk fever	- 4.2-6.8 mg/dl
Severe milk fever	- 3.5-5.7 mg/dl

Hypophosphatemia-

Normal serum P range is 4-8 mg/dl. In milk fever the P level is decreased to <3 mg/dl. Severe hypophosphatemia may be seen with serum P levels<1 mg/dl and may be associated with non-responsive milk fever cows.

Hyper/Hypomagnesemia-

Normal serum Mg value is 2-3 mg/dl, while in milk fever cases values vary from <2 mg/dl to >3 mg/dl. Hypermagnesemia is more commonly seen in milk fever (Radostits *et al.*, 2000). Low magnesium level may be associated with non-responsive milk fever cases.

Treatment

Initially there is discussion about previous or starting treatment concepts of milk fever, when etiology was not clear. In 1806, Price recommended the use of hot packs and blanketing to cause the affected cow to sweat profusely (Horst *et al.*, 1997). In 1814, Clater recommended prepartum bleeding (4 to 5 L/d for 8 to 10 d) (Horst *et al.*, 1997). Other treatments mentioned were pouring cold water on the head or rubbing the legs with cayenne pepper and alcohol. As summarized by Hibbs (1950), the first successful treatment for milk fever was proposed in 1897 when Schmidt suggested that milk fever was caused by a viral infection of the udder. To destroy the infection, he suggested that potassium iodide be injected into the udders of "infected" cows. This treatment reduced the mortality rate to 60 to 70%. Marshak (1956) later realized that these udder insufflation techniques prevented milk formation and, therefore, prevented the loss of Ca from plasma (Horst *et al.*, 1997).

Treatment during the first stage of the diseases, before the cow is recumbent, is the ideal situation (Radostits *et al.*, 2000).

- The treatment of choice for milk fever is slow, intravenous infusion of 8-12 g of calcium as soon as possible after the onset of clinical signs. Heart rate should be closely monitored for toxic effects. Calcium borogluconate containing products with or without added magnesium and phosphorus are mostly used in the India: usually 400 ml of 40% calcium borogluconate. For cattle 400-800 ml of 25% solution is the usual dose. Intravenous therapy to elevate calcium levels quickly is important to avoid downer cow syndrome, often seen when cows

are treated subcutaneously. Subcutaneous injection may be useful for maintaining blood levels. Solution containing dextrose should not be given subcutaneously because of abscess formation.

- During cold weather the solution should be warmed to body temperature. Warming the calcium solution seems to reduce toxic effects also.
- Approximately 85% of cases will respond to one treatment, in many cases cows recumbent from milk fever will rise within 10 minutes of treatment and others will get up 2-4 hours later.

It is essential to sit the cow in a sternal recumbency position and turn her so that she is lying on the side opposite to the one on which she was found. She should be turned to lie on the opposite side every two hours. Provide shelter or cover with rugs in exposed situations. If a response is not evident by 5-6 hours, the diagnosis should be reassessed, and, if necessary, a further intravenous infusion of 8-12 g of calcium administered. Relapses of milk fever occur in 25% of cases treated. Twelve hours after treatment, all calcium administered, whether by the intravenous or subcutaneous route, has been eliminated from the body. The treatment is only a holding operation until the normal adaptation process is in full operation. Cases of relapse usually occur at 18-24 hour intervals and should be treated in the same way. Removal of the calf and advice not to milk the cow for 24 hours except to check for the presence of mastitis may help to prevent relapses (Eddy, 1992). Massive dose of vitamin D (20-30 million unit daily) in feed in 5-7 days before parturition.

If hypomagnesaemia is a complicating factor of milk fever then the addition of the magnesium may be helpful. However, in cases of clinical hypomagnesaemia more than 1.0 g of magnesium will be required.

The presence of the phosphorus has no doubt been added because of the finding that the blood levels of phosphorus in cases of milk fever are also depressed. However, it has been shown that plasma phosphorus levels return to normal within a few hours after successful treatment with calcium borogluconate (CBG) without the addition of phosphorus.

Administration of ammonium chloride (@ 50-100 g/day, orally) produce acidosis and enhance blood calcium mobilization and ionization.

Prevention and Control

Prevention of milk fever is economically important to the dairy farmer because of reduced production loss, death loss, and veterinary costs associated with clinical cases of milk fever. In order to understand how to prevent this condition, one must understand why it becomes a problem. The onset of milk production drains on the animal's blood calcium levels and she is unable to replace this calcium. The body loses its ability to mobilize reserves of calcium in bone and absorb calcium from the gastrointestinal tract. As a result, hypocalcemia affects the cow's muscle contractions and rumen motility. The key to prevention of milk fever is management of a close-up dry cow or management during late pregnancy. The traditional way of preventing milk fever is to limit Ca intake during the dry period. This will allow the dry cow to adapt to Ca deficiency and make her better able to respond to milk Ca demand in early lactation.

Feeding high Ca forages (alfalfa hay and silage) should be restricted during the dry period. Replacing part or all of the alfalfa forages with grass hay or silage, cuts Ca consumption during the dry period and helps prevent milk fever. In cows fed limited amount of Ca and P during the dry period, bone and small intestine respond better to stimulation from parathyroid hormone and active vitamin D.

- Restricted Ca feeding to less than 50 g per day (less than 0.5% of the diet) during dry period.
- Phosphorus intake to less than 45 g per day (at 0.35% of the diet) during late pregnancy.

An important determinant of the risk for milk fever is the acid-base status of the cow at the time of parturition. Metabolic alkalosis predisposes cows to milk fever and sub clinical hypocalcemia. The traditional method of preventing milk fever in fresh dairy cows is to restrict dietary intake of Ca during the prepartum period. Cations have a positive charge like sodium (Na), potassium (K), calcium (Ca) and magnesium (Mg). Cations in the diet promote a more alkaline (higher blood pH) metabolic state which has been associated with an increased incidence of milk fever. Anions have a negative charge such as chloride (Cl), sulfur (S) and phosphorus (P). It has been discovered that milk fever can be effectively treated and/or prevented by feeding (dairy cows during the close up period (14 to 21 days pre-calving) a diet containing substantial amounts of negative ions (i.e. anionic salts) (Markandeya *et al.*, 2009).

Metabolic alkalosis impairs the physiologic activity of PTH and induces conformational changes in the PTH receptor, which prevents tight binding of PTH to its receptor. Anionic salts reduce the incidence of milk fever by increasing the mobilization of Ca from bones. They are helpful when there is a high incidence of milk fever or when it is difficult to control Ca consumption during the dry period. Anionic salts are effective in rations with high Ca levels (150 g per day). They should not be fed when Ca intake is low. Therefore it is very important to analyze feed ingredients especially forages, as book values on mineral content can be misleading. Urine pH is affected by changes in the cow's acid-base status and therefore, checking urine pH can help producers monitor the effectiveness of a ration containing anionic salts. It had been reported that addition of anionic salts reduced the incidence of clinical milk fever from 18.5% to 7.7% and the incidence of parturient hypocalcemia from 50.0% to 28.2%. When cations exceed anions in a solution the pH is increased and vice-versa (Table 3). Blood pH is ultimately determines by the number of positive and negative charges entering the blood from the diet. The major cations present in feeds and the charge they carry are Na^+, K^+, Ca^{2+} and Mg^{2+}. The major anions and their charges found in feeds are Cl^-, S^{2-}, P^{3-}. The difference between the number of cation and anion particles absorbed from the diet determines the general acid-base balance of the body and therefore, the pH of the blood. The cation-anion difference of the diet is commonly described in terms of mEq/kg of just sodium, potassium, chloride and sulfate as follows:

Dietary Cation-Anion Difference (DCAD)= (mEq Na^+ + mEq K^+) – (mEq Cl^- + mEq S^{2-})

This equation is useful, although it must be kept in mind that Ca, Mg and P, absorbed from the diet will also influence blood pH. Metabolic alkalosis is largely the result of a diet that supplies more cations (K, Na, Ca and Mg) than anions (Cl, SO_4 and PO_4) to the blood.

Table 3. Determination of DCAD on the basis of urine pH.

Ration DCAD	Urine pH (pre-fresh)	Acid-base status (pre-fresh)	Ca status (fresh)
Positive (>0 meq/kg)	8.0-7.0	Alkalosis	Low blood Ca
Negative (<0 meq/kg)	6.5-5.5 <5.5	Mild metabolic acidosis Kindney overload	Normal blood Ca

- Evade pre-calving milking.
- Removal of calf at birth with withdrawal only its colostrums needs by hand in the first 24 hours.
- Provide magnesium chloride in water.
- Prevent animals from becoming overfat and give them plenty of exercise.

KETOSIS AND FATTY LIVER

Ketosis is a production disease of dairy cows caused due to hypoglycaemia and is characterized by ketonaemia and ketonuria due increased level of ketone bodies in the blood. These ketone bodies are betahydroxybutyric acid, acetoacetic acid, and acetone (possibly also isopropanol). Most commonly, ketosis is seen either in high producing cows or cows on a poor diet. During the early eighties while some scientists were proposing to rename it as "post parturient hypoglycaemia" the emphasis for its cause has shifted to a deficiency in net energy rather than glucose. Biochemically the energy homeostasis has been intimately related not only to hypoglycaemia but also to the level of free fatty acids and influence of insulin, glucagon, somatotropin, thyroxin and glucocorticoids. Signs of the disease can be seen before calving, but they occur most commonly during the first 10 to 60 days after calving. The three-week period after calving seems to be the most critical time. Subclinical ketosis (SCK) is more important because it causes heavy economic losses due to reduced milk production. SCK is "a condition marked by increased levels of circulating ketone bodies without the presence of clinical signs of ketosis".

Blood glucose concentrations in clinically affected cows fall below the level required to support nerve and brain function and cows often exhibit stumbling while walking, head pressing, and other signs of central nervous system dysfunction. Ketotic cows also are inappetant, which further exacerbates their negative energy balance. Milk production falls precipitously (upsetting to the farmer, though this actually helps the cow cope with the negative energy balance situation). The type of ketosis described by Baird was readily cured by intravenous infusion of glucose, followed by the addition of energy in the form of grain to the diet (Goff, 2006).

Average worldwide milk production per cow has increased 1.25% per year for 20 years (Hibbit, 1979). Even as diets and management are improved to reduce ketosis in today's cows, future genetic improvements may continue to increase milk production and, therefore, lead to continued susceptibility of future cows.

The incidence of ketosis is higher in older cows and high-producing cows. As cows produce milk, they become more susceptible. In India incidence of ketosis has been recorded by various researchers varies from 4.22 to 50% and highest incidence during first 30 days of calving. Hibbitt (1979) reported that in some herds in the United Kingdom, up to 33% of cows tested positive for milk or urine ketones, lost weight, and had decreased milk production. Emery *et al.* (1964) reported that about 50% of the cows in some high-producing herds had at least subclinical ketosis and that 20 to 30% of the subclinical cases developed into clinical ketosis. Death from lactation ketosis is not common. Various sources suggest that in the US and Western Europe the incidence of the disorder lies within the range of 2 to 15% (Baird, 1982).

Importance

Ketosis is accompanied by fatty liver and cows that develop fatty liver and ketosis have reduced feed intake, lower gluconeogenic capacity (Grummer, 1995), lower milk production, and an increased risk for developing other metabolic and infectious diseases (Curtis *et al.*, 1985). Ketosis can be either clinical or subclinical; therefore, the incidence of ketosis and resulting financial losses are difficult to quantitate. Lactation ketosis is a worldwide problem in cows producing greatest amounts of milk. The average incidence has been about 4% in the United States and 2% in the United Kingdom (Schultz, 1968; 1974). With clinical ketosis, need for treatment and losses of milk production are obvious whereas with subclinical ketosis, neither is obvious, and the cow just ***"does not do well"***.

Financial losses are from decreased milk, decreased body weight, cost of treatment, disposal of cows that have recurring cases, and possibly death. If treatment, prevention, and other costs could be determined, an annual loss approaching $150 million for US dairymen is probable (Littledike *et al.*, 1981). Losses caused by undiagnosed subclinical ketosis exceed losses caused by clinical ketosis (Sharma *et al.*, 2009). Bovine ketosis is of substantial economic significance and has been found to be responsible for decline in milk production even two weeks before its clinical form, (Lucey *et al.*, 1986). Teli and Ali (2007) reported that the average drop in daily milk yield was 3.52 ±0.16 liters (36.70%) per day. Lactation ketosis will be difficult to eliminate. It has been estimated that an incident of ketosis costs the dairy producer $140/cow in treatment costs. Given a ketosis incidence rate of 17% in US cattle (Gillund *et al.*, 2001), a producer milking 120 cows would lose $2,520 annually to clinical ketosis. Subclinical ketosis costs approximately $78/case (Geishauser *et al.*, 2000). Additional losses are realized through lost milk production potential. Reducing subclinical ketosis and fatty liver such that cows produce a minimum of 0.5 kg more milk at peak lactation would result in an additional $2,880 of income. In addition, ketosis increases the risk of developing other metabolic diseases such as displaced abomasums ($334/case; Shaver, 1997), retained placenta ($319/case; Enevoldsen *et al.*, 1995), mastitis ($200/case; Nickerson, 1991) and other metabolic problems. Clearly, feeding management strategies that reduce clinical and subclinical ketosis will directly benefits dairy farm profitability, enhance animal well being and improve cow longevity (Varga, 2004).

Etiology

Specific biochemical and physiological causes of ketosis have not been proven. Baird *et al.* (Baired *et al.*, 1974) postulated that there is no single cause but that an inadequate nutrient supply, especially of energy, is a major factor.

Theories of ketosis development relate to glucose deficiency as a central theme; or glucose deficiency may be the primary theory; and various subtheories may deal with possible causes of glucose deficiency. This theory is logical because 60 to 85% of the available glucose is used in the mammary gland for milk synthesis (Bickerstaffe *et al.*, 1974).

As calving approaches, concentrations of progesterone in blood decrease and those of estrogen remain high or actually increase (Grummer, 1995). High circulating estrogen is believed to be one major factor that contributes to decreased dry matter intake (DMI) around calving (Grummer, 1993). During the last weeks of pregnancy, nutrient demands by the fetal calf and placenta are at their greatest (Bell, 1995), yet DMI may be decreased by 10 to 30% compared with intake during the early dry period. As lactation starts, glucose is essential for the formation of lactose (milk sugar) and milk fat. The requirement for glucose is at such high levels that the blood becomes low in glucose (hypoglycaemia). Fifty grams of glucose is required for each litre of milk with a 4.8% lactose test and 30 grams for each liter of milk with a 4% fat test. Because much of the dietary carbohydrate is fermented in the rumen, little glucose is absorbed directly from the digestive tract. Cows (and other ruminants) cannot be fed glucose in their diet; it has to be made in the rumen from suitable carbohydrates in the diet. If the amount of suitable carbohydrate in the diet is not enough to meet the glucose needs of the cow in full milk, the liver starts to manufacture glucose from other basic compounds in the body - usually fat reserves. Amino acids from the diet or from breakdown of skeletal muscle as well as glycerol from mobilized body fat contribute to glucose synthesis. The total intake of energy by cows after calving usually is less than energy requirements, even in healthy cows (Bell, 1995). Negative energy balance results in a high ratio of growth hormone to insulin in blood of cows, which promotes mobilization of long chain fatty acids from adipose tissue (body fat). If the amount of suitable carbohydrate in the diet is not enough to meet the glucose needs of the cow in full milk, the liver starts to manufacture glucose from other basic compounds in the body - usually fat reserves.

Fatty acids released from adipose tissue circulate as nonesterified fatty acids (NEFA), which are a major source of energy to the cow during this period. The concentration of NEFA in blood reflects the degree of adipose tissue mobilization (Pullen *et al.*, 1989); therefore, the greater the extent of negative energy balance, the more NEFA are released from body fat and the higher the concentration of NEFA in blood. The liver of cows takes up NEFA from the blood that flows through it. As the concentration of NEFA in blood increases around calving or in early lactation, more NEFA are taken up by the liver (Emery *et al.*, 1992). Unfortunately, if excessive, the release of NEFA from body fat overwhelms the capacity of the liver to use the fatty acids as fuel. They are instead converted to ketone bodies such as acetone, aceto-acetic acid, and *β*-hydroxybutyrate (BHBA).

Once taken up by the liver, NEFA can be: 1) completely oxidized to carbon dioxide to provide energy for the liver, 2) partially oxidized to produce ketone bodies that are released into the blood and serve as fuels for other tissues, or 3) reconverted to storage fat (triglycerides). Ruminants have an inherently low capacity for synthesis and secretion of very-low density lipoproteins to export triglyceride from the liver (Kleppe *et al.*, 1988; Pullen *et al.*, 1989), yet the rate of production of triglycerides in the liver is increased at the time of calving (Grum *et al.*, 1996). Cows fed typical diets during the dry period and transition period have an increased concentration of triglyceride in the liver 1 day after calving (Grum et al, 1996). If NEFA uptake by the liver becomes excessive, fatty liver may develop. Negative energy balance and carbohydrate insufficiency in the liver after calving leads to increased production of ketone bodies, which can result in ***"ketosis"***. Maintaining optimal liver function is central to the ability of cows to make a smooth transition into heavy milk production. As the degree of fatty infiltration increases, normal functions of the liver are affected adversely. In particular, fat infiltration impairs the ability of the liver to detoxify ammonia to urea (Strang *et al.*, 1998). Blood ammonia concentrations were positively correlated with the degree of fat accum ulation in the liver of cows shortly after calving (Zhu *et al.*, 2000). In severe fatty liver, normal functions of the liver are severely depressed, which results in the condition of *fatty liver syndrome* or *clinical fatty liver* (Morrow, 1976). Feed intake and carbohydrate status of the cow are important in determining the extent of body fat mobilization, fatty liver, and ketone body production in the liver. The sudden start of milk synthesis in the udder results in a tremendous demand for calcium. As a result, blood calcium concentrations can drop precipitously at calving, leading to milk fever. Smaller decreases in blood calcium, called subclinical hypocalcemia, are believed to be contributing factors in disorders, such as displaced abomasum and ketosis, by decreasing smooth muscle function, which is critical for normal function of the digestive tract (Goff and Horst, 1997).

Clinical signs

The composition of visible signs shown by ketotic cows has been lucidly described by Fox (Fox, 1971) and Schultz (Shultz, 1968; 1971). The cow first begins to dullness, depression, a staring expression, lose of appetite, pick at her feed, and leave some grain. She may progress from leaving most of the grain and some silage to the stage of eating only small amounts of hay and preferring to eat bedding. The further the ketosis develops, the greater is the development of perverted appetite. Concurrently, milk production is decreasing, and, in severe cases, decreasing dramatically. In mild cases, the only observation may be that the cow is not "doing well." In some cases there is nervous signs (Nervous ketosis) include false chewing movements, frothing and salivating profusely, pressing forward in the stanchion, walking in an unusual "goose-stepping" manner, licking themselves continuously (especially the forearms), grasping the side of the drinking cup with their mouths to the extent of inflicting injury to their tongue, lips, and dental pad and even loosening or breaking off several incisor teeth, and even demonstrate intermittently signs of mania. Hyperketonemia or hypoglycemia, or both, may lead to loss of appetite and perhaps also appearance of nervous signs. The decline in feed intake then would be expected to lead eventually to the observed decline in milk yield. The loss of body condition would be caused by rapid mobilization of adipose tissue, and also of protein stores, which provide gluconeogenic amino acids to support hepatic glucose production (Baird, 1982). In general the signs in clinical ketosis includes sudden drop in milk yield (100%) followed by selective feeding (78.94%) wasting (73.68%), depression (63.15%) and smell in breath/milk (47.46%) and these seem to be the principal signs with potential for utility in diagnosis of bovine ketosis under field conditions where laboratory facilities are limited or not available at all (Sharma *et al.*, 2009).

A few cows may become highly excitable. Breathing is shallow with an acetone smell in the breath. Cows will usually consume hay, straw or other roughage but generally refuse grain or concentrates. Ketosis may be either primary or secondary. Shaw (1956) advocated that ketosis that does not respond to glucocorticoids or glucose is secondary. With primary ketosis, body temperature does not increase. Causes of secondary ketosis include mastitis, metritis, displaced

abomasum, indigestion, retained placenta, nephritis, hardware disease, and extended milk fever. Nervous are seen in about 10% cases of primary ketosis. In India, ketosis mostly occurs in secondary form due to unhygienic farm conditions, as a result the case of pure primary ketosis, that to nervous ketosis either go unnoticed or not been diagnosed (Upadhyay *et al.*, 2008).

Diagnosis

1. History taking

History of recent calving, drastic decrease in milk production and type of feeding and extra supply of energy source and minerals.

2. Clinical signs

Decreased milk production, ketonic smell in urine and from mouth, reduced body weight etc.

3. Laboratory diagnosis

The blood level of total ketone bodies is the best indication of the ketotic status of the animal. Tests (Rothera test, Ketostrip) are available to check the ketone levels in the urine and milk. Milk has about half the ketone levels of blood whereas the ketone level in the urine exceeds the level in the blood by 4 times. Since urine is about 8 times more sensitive than milk. However, a negative urine test will not rule out ketosis.

The ketone test is a simple diagnostic tool for determining the presence of ketone bodies and is used by veterinarians and is also available to dairymen. The test is used for determining the presence of acetone in milk and urine. Colostrum milk does not give accurate results. The urine test shows positive results before the milk test does. Even so, do not be concerned until a positive test is obtained from milk. The blood level of ketone bodies is the best test for determining the degree of ketosis.

Qualitative test

Rothera test is the simple and cheap qualitative test for detection of ketone bodies. It is the modification of Ross test, details of the test is as follows-

Finally, the Ross modification of the Rothera test is run on the patient's urine. The reagent consists of 99 g of ammonium sulfate mixed with 1 g of sodium nitroprusside. Approximately 1 g of this mixture is added to 5 to 7 ml of urine in a standard test tube or 10 ml blood vial and, after dissolving, 1 ml of ammonium hydroxide solution or a flake of sodium hydroxide is added. After standing for 2-3 minutes, the test is read:

No color change	negative
Slight lavender	+
Deep lavender	++
Beet red or purple	+++
Deep beet red or purple and opaque (strongly positive)	++++

Quantitative test

- Drop in blood glucose level from normal of 50mg/dl to less than 40mg/dl.
- A rise in blood ketone to more than 10mg/dl to 100mg/dl Normal level 10mg/dl), urinary ketone increases to more than 70mg/dl.

Determination of blood beta-hydroxybutyrate-

It is difficult to subjectively assess the degree of subclinical ketosis problem (SCK) problems that a herd may be experiencing. Clinical ketosis rates are of extremely limited value at all in assessing the true ketosis status of a herd. The "gold standard" test for subclinical ketosis is blood BHB. This ketone body is more stable in blood than acetone or acetoacetate. Clinical ketosis generally involves much higher levels of BHBA (25 mg/dl or more).

The mostly commonly used cut-point for SCK is ≥1400 µmol/L (14.4 mg/dl) of blood BHB. Early lactation cows with blood BHB concentrations above this cut-point are at threefold greater risk to develop displaced abomasums or clinical ketosis, and cows with blood BHB concentrations above 2000 µmol/L are at risk for reduced milk yield. Some studies use a slightly lower cut-point (1200 µmol/L) of blood BHB for defining SCK. Clinical ketosis generally involves much higher levels of BHB (3000 µmol/L or more). The alarm level for the proportion of cows above the cut-point of 1400 µmol/L of blood BHB has not been well defined. Lowering BHBA below a threshold concentration is of little to no biological significance to the cow.

Blood BHB concentrations typically increase after feeding (Kronfeld *et al.*, 1968). Consistent sampling at 4 to 5 hours after the start of feeding has been suggested in order to capture peak BHB concentrations (Eicher *et al.*, 1998). The post-feeding peak in serum BHB concentrations is likely due to ruminal production of butyric acid. Excess amounts of butyric acid (either from ruminal production or from silage) are easily converted to BHB in the wall of the rumen.

Prevention

Occurrence of clinical ketosis as a herd problem is usually from faulty nutrition and management and should be minimized by following guidelines.

1. Overconditioned or fat cows are more susceptible to ketosis. Avoid excessive fattening before calving.
2. Avoid abrupt changes in the feeding program at calving time.

3. Provide properly balanced rations for heavy springers with increasing amounts of a high energy diet after calving.
4. Increase concentrate intake moderately in the late dry period but as rapidly after calving as possible and maintain intake
5. Provide adequate amounts (one-third of the dry matter) of good quality roughage.
6. Avoid feeding large amounts of silage to heavy springers.
7. Avoid silage high in butyric acid
8. Provide recommended amounts of protein, vitamins, and minerals.
9. Provide an environment for heavy springers and fresh cows that is comfortable and stimulates appetite.
10. Monitor milk ketones weekly for early detection.
11. Select cows with vigorous appetites.

Treatment

Radostits *et al.* (2000) essentially described therapy as a) replacement and b) hormonal. However, presently a combination of both is required. The various recommendations are as follows:

Glucose therapy:

- Dextrose 40%, give intravenously 500 ml. It has been suggested that 80% of 500 cc of 40% dextrose is eliminated in the urine within two hours after administration (Fox, 1971). Many cases are alleviated by this one treatment but, admittedly many others need more treatment, such as up to 1,500 ml initially, 500 ml daily (or every other day) for 2 to 5 to 7 times, or 2,000 ml given slowly by intravenous drip.
- Fructose. 0.5 g as 50% solution, intravenously.
- 500 g Oral glucose following premedication with sodium bi-carbonate-100 % recovery observed.

Sodium and Magnesium propionate- Give 80-200 g orally twice daily up to 10 days. Used as a preventive or as a "follow up" after initial intravenous injection of 500 ml of 40% dextrose. Good results but exerts destructive action on lung tissue if inhaled. Sodium and Magnesium propionate. Magnesium propionate stimulates insulin release, so it may be better anti-ketogenic than sodium propionate. Administration of propionate, which is a major glucogenic precursor, will tend to increase hepatic glucose output, but adminis- tration of glucose will tend to decrease it.

Propylene glycol- Propylene glycol 125 ml + 12 g of Niacin daily for 5-7 days. Used as a preventive or as a "follow up" after initial use of dextrose or glucocorticoids or both.

Glucose and hormones combined therapy:

The previous concepts of glucose therapy have failed to cure all the cases. Several workers have observed that simultaneous use of glucose and insulin to be a more effectively combination.

- 540 ml of Rintose + 80 units of insulin was better than Rintose alone.
- 20 % glucose + 0.5 units / kg insulin in buffaloes- recovery in 2 days.
- Comparative therapeutic trial of 25% glucose , glucose + insulin; glucose + Vetalog;Glucose + Vetalog + insulin and sod.propionate 60-80 g orally + 8g of nicotinic acid revealed glucose + insulin to be most effective.
- Corticosteriods (Tramcinolone acetonide)- Give 0.05 mg /kg b. wt. alone (33.33 % recovery). Glucocorticoid administration may or may not lead initially to a rise in glucose output, it seems probable that at 48 h after administration, at least, hepatic glucose output actually is decreased.
- Adrenocorticotropin- Give 200 to 800 units intramuscularly. Excellent results particularly in the prolonged or intermittent case and following the use of glucocorticoids previously (2 to 3 days).

Miscellaneous therapy:

- Vit.B_{12} and Cobalt to promate propionate production.
- Nicotinic acid 12 g daily to promote gluconeogenesis.
- Chloral hydrate. Give one ounce (28.5 g) twice daily for 3 to 5 days. (In nervous cases, sometimes necessary to give intravenously to be effective).

MASTITIS

Bovine mastitis, defined as .inflammation of the mammary gland, can have an infectious or non-infectious etiology (Bradley, 2002). It is characterized by physical, chemical and usually bacteriological changes in milk and pathological changes in glandular tissues (Radostits *et al.*, 2000). Because of their anatomical position are subject to outside influence and are prone to both inflammation and non-inflammatory conditions (Sharma, 2007). Infectious mastitis results from the introduction and multiplication of pathogenic microorganisms in the mammary gland and this leads to a reduced synthetic activity, changes in the milk composition, and elevated milk somatic cell count (SCC) (Harmon, 1994). Mastitis continues as a problem in many dairy herds despite proper application of proven control methods of teat dipping and total dry cow therapy. In general, mastitis is a complex disease dealing with, the interaction of microorganisms and the cow's anatomy and physiology, dairy husbandry and management, milking equipment and procedures and environment (Woods, 1986).

Several epidemiological studies have demonstrated that there is an association between the development of metabolic disease and subsequent development of mastitis. The prevalence of mastitis varies from 10 to 50%. Surveys of the prevalence of mastitis in most countries, irrespective of the cause, show a comparable figure of 50% among dairy cows and a quarter infection rate of 25% (Radostits *et al.*, 2000). Sharma *et al.* (2004) reported 70.32% incidence of subclinical mastitis in buffaloes, while Maiti *et al.* (2003) reported 70.37% incidence of subclinical mastitis in cows. Das and Joseph (2005) had been reported 84.31% prevalence of mastitis by cultural examination. In a study of NY dairies

(2,190 cows) there was a very strong association between parturient hypocalcemia or milk fever and mastitis. The odds ratio (multiplicative increases in occurrence) suggested that a milk fever cow was 8.1 times more likely to develop mastitis than a cow that had not had milk fever. The odds ratio for development of coliform mastitis was even greater (odds ratio, 9.0)(Curtis *et al.*, 1983). In a Swedish study, ketosis increased the risk of mastitis 2 fold (Oltenacu and Ekesbo, 1994).

Importance

Mastitis is the most economically important disease of dairy cattle, accounting for 38% of the total direct costs of the common production diseases (Kossaibati and Esslemont, 1997). Mastitis is a global problem as it adversely affects animal health, quality of milk and economics of milk production and every country including developed ones suffer huge financial losses (Sharma *et al.*, 2007). Mastitis reduces milk and milk products in all dairy producing countries of the world (International Dairy Federation, 1999). It is the most important deadly disease of dairy animals is responsible for heavy economic losses due to reduced milk yield (up to 70%), milk discard after treatment (9%), cost of veterinary services (7%) and premature culling (14%). In India, annual economic losses incurred by dairy industry on account of udder infections have been estimated about Rs.6053.21 crore. Out of this, loss of Rs. 4365.32 crore (70 % - 80 % loss) has been attributed to sub clinical version of udder infections (Dua, 2001). In addition to heavy losses in milk quality and quantity, it also causes irreversible damage to the udder tissue and less occasional fatalities (Radostits *et al.*, 2000). Mastitis can lead to the reduction of offspring to a given production system due to the insufficient milk production resulting in starvation.

It has been estimated that annual economic losses due to mastitis in the US, $1.5 to 2.0 billion. Losses from subclinical mastitis of lost milk production and higher cow replacements costs associated with high somatic cell counts were estimated at $960 million. Because of the recognition of the importance of mastitis, the vast majority of US

dairy producers use recommended management practices for mastitis prevention such as teat dipping and dry cow treatment (USDA, 1996).

Apart of its economic importance it also carries public health significance (Sharma *et al.*, 2003). Milk from mastitic cows may contain harmful pathogenic microorganisms to human beings. Bad milk would be responsible for more sickness and deaths (Howard, 1993). Although, pasteurisation has eliminated the gross public health significance of milk, there are still enough consumers of raw milk to mention the various mastitis or milk related factors affecting human health. In recent years a human group B streptococcus, not dissimilar to *Streptococcus agalactiae* has been reported as a causes of meningitis and death in newborn infants and also urinogenital tract infection in adults (Woods, 1986). There has also been reported of individuals taken ill after consuming milk products high in toxins produced by *Staphylococcus aureus* that pasteurization did not eliminate. Besides *Escherdichia coli* can cause enteritis, diarrhoea and vomiting (Woods, 1986). Diseases like Tuberculosis, Brucellosis, Listeriosis, and Q-fever may be transmitted through milk to human beings (Hugh-Jones *et al.*, 1995) and *Cryptococccus neoformans* and *prototheca* species also have zoonotic importance (Rebhun, 1995).

Etiology

Mastitis is a multietiological complex disease. The cow udder is an ideal environment for microbial growth and under optimum udder conditions, such as temperature, nutrition, and freedom from outside influence, pathogenic organisms multiply astronomically and it is this factor that causes udder damage and triggers the response that is recognized as mastitis. More than 200 infectious causes of bovine mastitis are known to date and in large animals the commonest pathogens are *Staphylococcus aureus*, *Streptococcus agalactiae*, other *streptococcus* and Coliforms. It may also be associated with many other organisms including *Actinomyces pyogenes*, *Pseudaomonas aeruginosa*, *Nocardia asteroides, Clostridium perfringens*, and others like *Mycobacterium, Mycoplasma, Pastuerella* and *Prototheca* species and *yeasts*. The majority of the cases are caused by only a few common bacterial pathogens, namely, *Staphylococcus* species, *Streptococcus* species, Coliforms, and *Actinomyces pyogenes*.

Many workers from India have been reported that *Staphylococcus* spp. is the chief etiological agent of mastitis in cattle and buffaloes (Sharma *et al.*, 2007a; Sharma, 2008; Sharma *et al.*, 2007b). A study in Jammu by Sudhan *et al.* (2005) suggests that *Staphylococcus aureus* (56.89%) is major pathogen followed by *Micrococcus* spp. (15.51%), *Bacillus cereus* (12.06%), *Staphylococcus epidermidis* (8.62%), *Klebsiella* spp. (3.44%), *Escherichia coli* (1.72%), and *Corynebacterium* spp. (1.72%). *Staphylococcus aureus* present in the udders of chronically infected cows and also in cuts and chaps on the teat skin, *Streptococcus agalactiae* found only in the udder, though it can survive for 2-3 weeks away from the cow without multiplication and *Streptococcus dysgalactiae* found in the udder and on teat skins are the main pathogenic bacteria that are involved in contagious mastitis (Radostits *et al.,* 2000). *Streptococcus uberis* is found in the mouth, vulva, teats and faeces of the cows as well as the environment. It is probably the common cause of environmental mastitis with less severe clinical signs than *Escherichia coli*. *E. coli* can cause severe even fatal mastitis moreover *E. coli* enormously present in the faeces and passes out to contaminate the environment and can multiply to greater concentrations away from the cow. Some species like *Pseudomonas*, *Klebsialla* and yeasts are pathogens that are considered as causal agents to environmental mastitis. *Actinomyces pyogenes*, *Streptococcus dysgalactiae* and *Peptococcus indolicus* are bacterial agents that are involved in summer mastitis, which seen especially in pregnant cows and heifers although it can also occur in non-pregnant animals.

Clinical signs

Mastitis can be classified (Griffin *et al.*, 1987) according to its duration; acute (recent debut) or chronic (debut long time ago), or according to the presence or absence of clinical signs; clinical or subclinical. In clinical mastitis, there is one or more visible inflammatory signs (e.g. swelling, hot, redness, pain, hardness) present in the udder or in the milk (e.g. watery, flakes, clots, pus, blood), the milk composition may be abnormal and the somatic cell count (SCC) is increased. During a subclinical mastitis, the udder and milk shows no visible sign of inflammation but the milk composition is altered, specially the lactose content is decreased, while the SCC is increased (Bramley, 1992). In chronic form, no systemic signs and hardness of quarter(s) may or may not be present, sometimes fibrosis and yellow coloured/watery

milk with flakes or custard like. An inflammatory process that persists over many months or from one lactation period to the next is called chronic mastitis. Grossly, the affected tissue is tough and smaller than normal (due to proliferation of fibrous connective tissue and glandular atrophy).

Diagnosis

Diagnosis of mastitis should be performed in step-wise-step. It should be started from physical examination of udder to cultural examination. For details see another chapter on mastitis in this book.

Physical examination of udder-

This is the first step to examine the case of mastitis. Abnormal lobulation or contour can see by this method. The results of the physical examination, when correlated with other observations, facilitate the clinician for a complete diagnosis. Physical examination of each gland must be made on the empty udder. The most opportune time, therefore, is immediately after milking when the hormone stimulation has ceased and the udder is completely relaxed (Sharma *et al.*, 2009). By visual observation or inspection clinician can observe so many undesirable features like udder symmetry (e.g. oat like, rounded, step shaped and pendulous udder) and, teat shape and placement which can help in the confirmatory diagnosis.

Examination of milk-

Before conduction of any mastitis test, the freshly drawn milk should be examined by necked for the visible abnormalities (like clots, flakes, blood, pus etc.) in the milk. During examination age and stage of lactation should be kept in mind, in dry period milk changes to watery. There are various indirect mastitis tests are available for the diagnosis of mastitis at early stage i.e. subclinical mastitis for example- California mastitis test (CMT), White Side test (WST), Surf field mastitis test, Sodium lauryl sulphate test, mastrip test, Bromothymol blue test, somatic cell count (SCC) etc.

CMT and surf field mastitis tests are cheap, fast and easy to perform. The principle of both the tests is similar i.e. as surfactant. Take equal quantity of milk and reagent and mix it in a CMT paddle (by rotation). If there is formation of gel within 1 minute, indicate the positive for mastitis and in case of negative, the mixture remains normal or no change in consistency or gel formation. On the basis gel formation, grade the severity of infection.

Cultural examination

This is the purely laboratory diagnostic test which required various chemicals, media, glassware and technical skill and time consuming. Collect the milk samples in sterile vials and inoculate on different media for cultural isolation and identification of microorganism.

Treatment

Since mastitis results in the destruction and disturbances of the mammary gland and affects milk production and productivity, it needs serious and immediate action as soon as possible. Among the many actions that could be taken as treatment, the administration of antimicrobial agents is the most commonly used method. The emphasis of clinical mastitis treatment has been on antimicrobial therapy and currently there are a number of conventional antibiotics with different degree of spectrums that are used for the treatment of the disease in India. Pathogenic microorganims are sensitive to one or more antimicrobial agents and at the same time are resistant to one or a number of conventional drugs. An important aspect of mastitis therapy is the alleviation of inflammation that can result swelling and subsequent pain associated with clinical mastitis that can cause considerable discomfort to the cow in the udder. Then the purpose of mastitis therapy is to assist the affected quarter to clear infection as rapidly as possible and to enable a quick return of the cow to normal milk production (Fitzpatrick *et al.*, 1998). The conventional antimicrobial agents used in mastitis treatment include penicillin, cloxacillin, erythromycine, cephalosporins, gentamycin, amikacin, trimethoprim-sulfa, amoxycillin-clavulanic acid, polymyxin B, cephalotin, tetracycline, ampicillin, neomycin, kanamycin, nystatin, miconazole and other drugs with systemic injectable and local intramammary infusion formulations.

Anti-inflammatory

Anti-inflammatory drugs are widely used to treat acute clinical cases of mastitis. In India, previously Diclofenac sodium was commonly used as anti-inflammatory drug but now it has been banned due to residual effect in treated carcass. Presently meloxicam is commonly used as anti-inflammatory in the treatment of mastitis at the dose rate of 0.5 mg/kg b. wt. intramuscularly.

Steroids

Glucocorticoid drugs inhibit the production of inflammatory molecules and the adhesion molecules that facilitate transport of inflammatory cells from the bloodstream to the site of inflammation. Glucocorticoids also help maintain microcirculation and cell membrane integrity, interfere with dissolution and disruption of connective tissue, decrease formation of histamine by injured cells, and antagonize toxins and kinins. These actions of glucocorticoid drugs could be expected to be of benefit to the mastitic cow, particularly one with mastitis caused by endotoxin-producing coliform bacteria (O'Rourke and Baggot, 2004). Glucocorticoids need to be administered early in the course of disease for maximum efficacy. Intramuscular administration of Dexamethasone @ 30 mg (as total dose for adult cow) is sufficient.

Oxytocin

Oxytocin @ 40-50 IU per animal per day intramuscularly. Oxytocin facilitate complete milk evacuation and to remove toxic material and debris).

Supportive therapy-

Vitamin C (Ascorbic acid)- @ 25mg/kg b. wt. in the management of subclinical mastitis.

Vitamin E and Selenium- Sharma *et al.* (2007) have been reported that dietary supplementation of vitamin E (500 IU/animal/day) and Selenium (6 mg/animal/day) effective for the treatment and control of subclinical mastitis in lactating dairy cows. Vitamin E and Selenium in combination is also available in injection form (E-care-Se).

Fluid therapy

Isotonic fluids containing glucose and antihistaminic are to be used in peracute and acute cases with extensive tissue damage and toxemia. Intravenous infusion of hypertonic saline (7.5% NaCl) @ 2ml/45kg b. wt. is useful in the treatment of acute mastitis. Intramammary administration of 0.5-1.0 liter of hypertonic saline in affected quarter once a day after milking for 2-3 days is clear the 50-60% of the clinical symptoms. Application of cold (ice bags) reduces the absorption of toxins in peracute and acute cases of mastitis.

Prevention and Control

Implementation of mastitis control strategies has led to a change in the incidence and etiology of mastitis over the past 40 years. This change has resulted in a decrease in the prevalence of contagious mastitis pathogens and an increase in the relative, and arguably absolute, importance of the environmental pathogens such as *Streptococcus uberis* and *E. coli* on the vast majority of well-managed dairy units. The following points should be considered for prevention and control of mastitis at farm-

- ☞ Proper cleaning of animal shed.
- ☞ Animal shed should be ventilated.
- ☞ Avoid over crowding.
- ☞ Proper cleaning of milker's hand.
- ☞ Washing of udder before milking.
- ☞ Regular checkup and cleaning of milking machine.
- ☞ Avoid knuckling method of hand milking.
- ☞ Healthy animals should be milked first.
- ☞ Complete milking of the animal.
- ☞ Adopt pre- and post- milking teat dipping.
- ☞ Regular screening of animals for mastitis.
- ☞ Dry cow therapy.
- ☞ Vaccination against major mastitis pathogens like *Staphylococcus aureus* and *E. coli* mastitis.

REFERENCE

Amano, H., Takesima, Y., Nitta, M., Mabuti, T., Tokuti, T. and Yagi, T. (1992). Relationship of haematocrit values with age, lactation stage, nutrition levels of dairy cows and temperature. J. Jpn. Vet. Med. Assoc., 45: 467-470.

Baird, G.D. (1982). Primary Ketosis in the High-Producing Dairy Cow: Clinical and Subclinical Disorders, Treatment, Prevention, and Outlook. J. Dairy Sci., 65(1): 1-10.

Baird, G.D., Heitzman, R.J., Hibbitt, K.G. and Hunter, G.D. (1974). Bovine ketosis: A review with recommendations for control and treatment. Part I. Brit. Vet. J., 130: 214.

Bauman, D.E. and Currie, W.B. (1980). Partitioning of nutrients during pregnancy and lactation: a review of mechanisms involving homeostasis and homeorhesis. J. Dairy Sci., 63: 1514-1529.

Bell, A.W. (1995). Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. J. Anim. Sci., 73: 2804-2819.

Bickerstaffe, R., Annison, E.F. and Linzell, J.L. (1974). The metabolism of glucose acetate, lipids, and amino acids in lactating dairy cows. J. Agric. Sci., Camb., 82: 71.

Blowey, R.W. (1975). A practical application of metabolic profiles. Vet. Rec., 97: 324-327.

Bradley, A. (2002). Bovine mastitis: an evolving disease. The Veterinary Journal 164, 116-128.

Bramley, A.J. (1992). Mastitis and machine milking. In: Bramley, A.J., Dodd, F.H., Mein, G.A. and Bramlet, J.A. (eds.) Machine Milking and Lactation, Insight Books, USA. Pp. 343-372.

Commodityonline (2008). India milk output to reach 111 mtn by 2010 17 September 2008 www_commodityonline_com.htm

Curtis, C.R., Erb, H.N., Sniffen, C.J., Smith, R.D. and Kronfeld, D.S. (1985). Path analysis of dry period nutrition, postpartum metabolic and reproductive disorders, and mastitis in Holstein cows. J. Dairy Sci., 68: 2347-2360.

Curtis, C.R., Erb, H.N., Sniffen, C.J., Smith, R.D., Powers, P.A., Smith, M.C., White, M.E., Hillman, R.B. and Pearson, E.J. (1983). Association of parturient hypocalcemia with eight periparturient disorders in Holstein cows. J. Am. Vet. Med. Assoc., 183(5): 559-561.

Das, P.K. and Joseph, E. (2005). Identification and antibigram of microbes associated with buffalo mastitis in jabalpur, madhya pradesh, India. Buff. Bull., 24 (1): 3-9.

Dua, K. (2001). Incidence, etiology and estimated economic losses due to mastitis in Punjab and in India- An update. Indian Dairyman, 53(10): 41-48.

Duffield, T.F. (2004). Monitoring strategies for metabolic disease in transition dairy cows. In: Proc 23rd World Buiatrics Cong, Quebec, Quebec, Canada, July 11-16, pp. 34-35.

Dufflied, T.F. (2006). Epidemiology of subclinical production diseases in dairy cows with an emphasis on ketosis. In: Proc. of 12th Intl. Conf. on Production diseases in farm animals by Joshi, N. and Herdt, T.H.,. 126-135.

Dunklee, J.S., Freeman, A.E. and Kelley, D.H. (1994). Comparison of Holsteins selected for high and average milk production. 2. Health and reproductive response to selection for milk. J. Dairy Sci., 77: 3683-3690.

Eddy, R.G (1992). Major metabolic disorders. In: Bovine medicine – diseases and husbandry of cattle. Blackwell Scientific Publications.

Eicher, R., Liesegang, A., Bouchard, E., *et al.* (1998). Influence of concentrate feeding frequency and intrinsic factors on diurnal variations of blood metabolites in dairy cows. Proc. Am. Assoc. Bov. Pract., 31: 198-202.

Emery, R.S., Burg, N., Brown, L.D. and Blank, G.N. (1964). Detection, occurrence, and prophylactic treatment of borderline ketosis with propylene glycol feeding. J. Dairy Sci., 47: 1074.

Emery, R.S., Liesman, J.S. and Herdt, T.H. (1992). Metabolism of long chain fatty acids by ruminant liver. J. Nutr., 122: 832-837.

Enevoldsen, C., Sorensen, J.T., Thysen, I., Guard, C. and Grohn, Y.T. (1995). A diagnostic and prognostic tool for epidemiologic and economic analyses of dairy herd health management. J. Dairy Sci., 78: 947-961.

Erb, H.N. and Martin, S.W. (1978). Age, breed and seasonal patterns in the occurrence of ten dairy cow diseases: a case control study. Can. J. Comp. Med., 42: 1.

Fitzpatrick, J.L., Young, F.J., Eckersall, D. Logue, D.N., Knight, C.J. and Nolan, A. (1998). Recognizing and controlling pain and inflammation in mastitis. In Proceedings of the 10th British Mastitis Conference, Stoneleigh, October 7,1998. 36-44.

Fox, F.H. (1971). Clinical diagnosis and treatment of ketosis. J. Dairy Sci., 54: 974.

Geishauser, T.K., Leslie, K., Tenhag, J. and Bashiri, A. (2000). Evaluation of eight cow-side ketone tests in milk for detection of subclinical ketosis in dairy cows. J. Dairy Sci., 83: 296-299.

Gillund, P., Reksen, O., Gröhn, Y.T. and Karlberg, K. (2001). Body condition related to ketosis and reproductive performance in Norwegian dairy cows J. Dairy Sci., 84: 1390-1396.

Goff, J.P. (2006). Macromineral physiology and application to the feeding of the dairy cow for prevention of milk fever and other periparturient mineral disorders. Anim. Feed Sci. Tech., 126: 237-257.

Goff, J.P. (2006). Major advances in our understanding of nutritional influences on bovine health. J. Dairy Sci., 89(4): 1292–1301.

Goff, J.P. and Horst, R.L. (1997). Effect of addition of potassium or sodium, but not calcium, to prepartum rations induces milk fever in dairy cows. J. Dairy Sci., 80: 176.

Goff, J.P. and Horst, R.L. (1997). Physiological changes at parturition and their relationship to metabolic disorders. J. Dairy Sci., 80: 1260– 1268.

Goff, J.P., Horst, R.L. and Reinhardt, T.A. (1987). The pathophysiology and prevention of milk fever. Vet. Med., 82: 943.

Goff, J.P., Horst, R.L., Mueller, F.J., Miller, J.K., Kiess, G.A. and Dowlen, H.H. (1991). Addition of chloride to a prepartal diet high in cations increases 1,25-dihydroxyvitamin D response to hypocalcemia preventing milk fever. J Dairy Sci., 74: 3863-3871.

Goff, J.P., Kehrli, Jr. M.E. and Horst, R.L. (1989). Periparturient hypocalcemia in cows: prevention using intramuscular parathyroid hormone. J. Dairy Sci., 72: 1182.

Goff, J.P., Reinhardt, T.A. and Horst, .R.L. (1995). Milk fever and dietary cation-anion balance effects on concentration of vitamin D receptor in tissue of periparturient dairy cows. J. Dairy Sci., 78: 2388-2394.

Griffin, T.K., Morant, S.V. and Dodd, F.H. (1987). Bovine mastitis. Definition and guidelines for diagnosis. Bulletin of the International Dairy Federation (IDF) No. 211: 2-24.

Grum, D.E., Drackley, J.K., Younker, R.S., LaCount, D.W. and Veenhuizen, J.J. (1996). Nutrition during the dry period and hepatic lipid metabolism of periparturient dairy cows. J. Dairy Sci., 79: 1850-1864.

Grummer, R.R. (1993). Etiology of lipid-related metabolic disorders in periparturient dairy cows. J. Dairy Sci., 76: 3882-3896.

Grummer, R.R. (1995). Impact of changes in organic nutrient metabolism on feeding the transition dairy cow. J. Anim. Sci., 73: 2820-2833.

Hansen, L.B. (2000). Consequences of selection for milk yield from a geneticist's viewpoint. J. Dairy Sci., 83: 1145-1150.

Harmon, R.J. (1994). Physiology of Mastitis and Factors Affecting Somatic Cell Counts. J. Dairy Sci., 77: 2103-2112.

Herdt, T.H., Dart, B. and Neuder, L. (2001). Will large dairy herds lead to the revival of metabolic profile testing?. In: Proc. Am. Assoc. Bov. Pract. 34: 27-34.

Hibbitt, K.G. (1979). Bovine ketosis and its prevention. Vet. Rec., 105: 13.

Hibbs, J.W. (1950). Milk fever (parturient paresis) in dairy cows: a review. J. Dairy Sci., 33: 758.

Hoeben, D., Heyneman, R. and Burvenich, C. (1997). Elevated levels of -hydroxybutyric acid in periparturient cows and in vitro effect on respiratory burst activity of bovine PMN's. Vet. Immunol. Immunopathol., 58: 165-170.

Hoff, B. and Duffield, T. (2009). Nutritional and metabolic profile testing of dairy cows. AHL Lab Note, No.4., pp.1-3.

Horst, R.L., Goff, J.P. and Reinhardt, T.A. (1990). Advancing age results in reduction of intestinal and bone 1,25-dihydroxyvitamin D receptor. Endocrinology, 126: 1053.

Horst, R.L., Goff, J.P. and Reinhardt, T.A. (1994). Calcium and vitamin D metabolism in the dairy cow. J. Dairy Sci., 77: 1936.

Horst, R.L., Goff, J.P., Reinhardt, T.A. and Buxton, T.R. (1997). Strategies for preventing milk fever in dairy cattle. J. Dairy Sci. 80:1269-1280.

Howard, J.L. (1993). Current Veterinary Therapy 3. Food Animal Practice. Philadelphia: W.B. Sounders Company, Harcourt Brace Jovanovich, inc.. pp 762-763.

Hugh- Jones, M.E., Hubbert, W.T. and Hagstard, H.V. (1995). Zoonoses: Recognition, Control and Prevention. 1st ed. Iowa. Iowa State University Press, USA, pp 262-300.

Ingraham, R.H. and Kappel, L.C. (1988). Metabolic profile testing. Vet Clinics North Am. Food Anim. Pract., 4(2): 391.

Ingvartsen, K.L., Dewhurst, R.J. and Friggens, N.C. (2003). On the relationship between lactational performance and health: is it yield or metabolic imbalance that cause production disease in dairy cattle? A position paper. Livest. Prod. Sci., 83: 277-308.

International Dairy Federation (1999). Brussels, Belgium. No 333/1999.

Jones, W.P., Hansen, L.B. and Chester-Jones, H. (1994). Response of health care to selection for milk yield of dairy cattle. J. Dairy Sci., 77: 3137-3152.

Jonsson, G. (1960). On the etiology and pathogenesis of parturient paresis in dairy cows. Acta. A.gric. Scand., (Suppl.) 8: 1.

Jonsson, N.N. and Daniel, R.C.W. (1997). Effects of hypocalcaemia on blood flow to the ovaries of sheep. J. Vet. Med. A, 44: 281-287.

Kimura, K., Goff, J.P. and Kehrli Jr., M.E. (1999). Effects of the presence of the mammary gland on expression of PMN adhesion molecules and myeloperoxidase activity in periparturient dairy cows. J. Dairy Sci., 82:2385-2392.

Kleppe, B.B., Aiello, R.J., Grummer, R.R. and Armentano, L.E. (1988). Triglyceride accumulation and very low density lipoprotein secretion by rat and goat hepatocytes in vitro. J. Dairy Sci., 71: 1813-1822.

Klucinski, W., Degorski, A., Miernik-Degorska, E., Targowski, S. and Winnicka, A. (1988). Effect of ketone bodies on the phagocytic activity of bovine milk macrophages and polymorphonuclear leukocytes. Zentralblatt für Veterinärmedizin, 35: 632–639.

Kossaibati, M.A. and Esslemont, R.J. (1997). The costs of production diseases in dairy herds in England. The Vet. J., 154, 41-51.

Kremer, W.D., Noordhuizen-Stassen, E.N., Grommers, F.J., Schukken, Y.H., Heeringa, R., Brand, A. and Burvenich, C. (1993). Severity of experimental Escherichia coli mastitis in ketonemic and nonketonemic dairy cows. J. Dairy Sci., 76: 3428-36.

Kronfeld, D.S., Raggi, F. and Ramberg, C.F.Jr: (1968). Mammary blood flow and ketone metabolism in normal, fasted, and ketotic cows. Am. J. Physiol., 215: 218-227.

Kusumanti, E., Agger, J. F. and Jensen, K. (1993). Association between incidence risk of milk fever and lactation number, breed and season. Acta. Vet. Scand., S89: 141.

Lavor, P., Brochart, M. and Theret, M. (1961). Enquete sur lafieure vitulaire et al tetanie d'herbage des bovins en France. Econ. Med. Anita., 2: 5.

LeBlanc, S.J. (2006). Monitoring programs for transition dairy cows. In: Proceedings 24th World Buiatrics Congress, October 15-19, Nice, France, pp. 460-471.

Littledike, E.T. (1974). Parturient hypocalcemia, hypomagnesemia, mastitis-metritis-agalactia complex of swine. Page 335 in Lactation – A comprehensive treatise. Vol. II. B. L. Larson and V. R. Smith, ed. Academic Press, New Vork, NY.

Littledike, E.T., Whipp, S.C. Witzel, D.A. and Baetz, A.L. (1970). Insulin corticoids and parturient paresis. Academic Press, New York.

Littledike, E.T., Young, J.W. and Beitz, D.C. (1981). Common metabolic iseases of cattle: ketosis, milk fever, grass tetany, and downer cow complex. J. Dairy Sci., 64(6): 1465-1482.

Lucey, S., Rowlands, G.J. and Russell, A.M. (1986). Short term association between diseases and milk yield in dairy cows. J. Dairy Res., 53: 7-15.

Maiti, S.K., Sharma, Neelesh and Awasthy, B.K. (2003). Studies on sub clinical mastitis in cattle and buffaloes of Durg area of Chhattisgarh. Vet. Practitioner. 4(2): 90.

Markandeya, N.M., Patil, A.D. and Bharkad, G.P. (2009). Intas Polivet, 10(1): 13-19.

Marshak, R.R. (1956). Studies on parturient paresis in dairy cows with particular reference to udder insufflation. J.Am.Vet. Med. Assoc., 128: 423.

Morrow, D.A. (1976). Fat cow syndrome. J. Dairy Sci., 59: 1625.

Mulligan, F., O'Grady, L., Rice, D. and Doherty, M. (2006). Production diseases of the transition cow: Milk fever and subclinical hypocalcaemia. Irish Vet. J., 59(12): 697-702.

Mulligan, F.J. and Doherty, M.L. (2008). Production diseases of the transition cow. The Vet. J., 176: 3-9.

Nickerson, S.C. (1991). Mastitis control in heifers and dry cows. Dairy Food & Environ. Sanit., 11: 438-443.

O'Rourke, D.J. and Baggot, J.D. (2004). Antimicrobial Therapy of Mastitis. In: text book of Bovine Medicine- Diseases and Husbandry of Cattle by Andrews, A.H., Blowey, R.W., Boyd, H. and Eddy, R.G., 2nd edn., Blackwell Publishing Company, UK. Pp. 391-405.

Oetzel, G.R. (2004). Monitoring and testing dairy herds for metabolic disease. Vet Clinics North Am. Food Anim. Pract., 20: 651-674.

Okada, K. and Yasuda, J. (2001). Methods for collection and preservation of cattle blood for metabolic profile test. Jpn. J. Large Anim. Clin., 24(1): 13-18.

Oltenacu, P.A. and Ekesbo, I. (1994). Epidemiological study of clinical mastitis in dairy cattle. Vet. Res., 25: 208-812.

Payne, J.M. (1966). The importance of cattle diseases in the United Kingdom in relation to the research carried out upon them. Brit. Vet. Nutr., 122: 183.

Payne, J.M. (1972). Production disease. J. Royal Agric. Soci. England, 133: 69-86.

Payne, J.M., Dew, S.M., Manston, R. and Faulks, M. (1970). The use of a metabolic profile test in dairy herds. Vet. Rec., 87: 150-158.

Pryce, J.E., Nielsen, B.L., Veerkamp, R.F. and Simm, G. (1999). Genotype and feeding system effects and interactions for health and fertility traits in dairy cattle.Livestock Production Science 57(3): 193-201.

Pullen, D.L., Palmquist, D.L. and Emery, R.S. (1989). Effect on days of lactation and methionine hydroxy analog on incorporation of plasma fatty acids into plasma triglycerides. J. Dairy Sci., 72: 49-58.

Radostits, O.M., Gay, C.C., Blood, D.C. and Hinchkliff, K.W. (2000). Veterinary Medicine. 9th edn. ELBS & Baillier Tindall. pp.563-618.

Rajala-Schultz, P.J., Gröhn, Y.T. and McColloch, C.E. (1999). Effects of milk fever, ketosis, and lameness on milk yields in dairy cows. J. Dairy Sci. 82: 288-294.

Rebhun, W.C. (1995). Disease of Dairy Cattle. Williams and Wilkins. Baltimore. Philadelphia: Lea and Fibiger. USA. pp 279-294.

Rowlands, G.J. (1980). A review of variations in the concentrations of metabolites in the blood of beef and dairy cattle associated with physiology, nutrition and disease, with particular reference to the interpretation of metabolic profiles. Wld. Rev. Nutr. Diet., 35: 172-235.

Rukkwamsuk, T., Kruip, T.A. and Wensing, T. (1999). Relationship between overfeeding and over conditioning in the dry period and the problems of high producing dairy cows during the postparturient period. Vet. Quarterly, 21: 71–77.

Schultz, L.H. (1968). Ketosis in dairy cattle. J. Dairy Sci., 51: 1133.

Schultz, L.H. (1971). Management and nutritional aspects of ketosis. J. Dairy Sci., 54:962.

Schultz, L.H. (1974). Ketosis. Page 317 in Lactation. Vol. II. Biosynthesis and secretion of milk/diseases. B. L. Larson and V. R. Smith, ed. Academic Press, New York, NY.

Sharma, Neelesh (2003). Epidemiological study on sub clinical mastitis in dairy animals: Role of vit E and Selenium supplementation on its control in cattle. M.V.Sc. thesis, IG.KVV., Raipur (C.G.) India.

Sharma, Neelesh (2007). Alternative approach to control intramammary infection in dairy cows- A review. Asian J. Anim. Vet. Adv.., 2(2):50-62.

Sharma, Neelesh (2008). Foot and Mouth Disease - Mastitis Cascade in Dairy Cattle: A field study. Intnl. J. Zoolog. Res., 4(1): 64-67.

Sharma, Neelesh, Gupta, S.K., Sharma, U. and Hussain, K. (2007b). Treatment of clinical mastitis in buffalo-A case report. Buffalo Bulletin. 26(2): 56-58.

Sharma, Neelesh, Gupta, S.K., Soodan, J.S. and Singh, R. (2006). Important production diseases of dairy animals-A review. Dairy Planner, 2(11): 6-8.

Sharma, Neelesh, Maiti, S.K. and Koley, K.M. (2004). Studies on the incidence of sub clinical mastitis in buffaloes of Rajnandgaon district of Chhattisgarh state. Vet. Practitioner. 5(2):123-124.

Sharma, Neelesh, Maiti, S.K. and Roy, S. (2003). Role of vitamin E in the control of mastitis in dairy cows. Vet. Practitioner, 4(2): 140-143.

Sharma, Neelesh, Maiti, S.K. and Sharma, K.K. (2007a). Prevalence, etiology and antibiogram of microorganisms associated with sub clinical mastitis in buffaloes in Durg, Chhattisgrh State (India). International J. Dairy Sci., 2(2): 145-151.

Sharma, Neelesh, Pandey, V. and Upadhya, S.R. (2009). Recent trends in the diagnosis of bovine mastitis under field condition. Indian Dairyman, 61(4): 21-27.

Sharma, Neelesh, Singh, R. and Hussain, K. (2005). Milk fever in dairy cows. Dairy Planner, 2(3): 41-42.

Sharma, Neelesh, Upadhyay, S.R. and Srivastava, A.K. (2009). Bovine ketosis-An overview. Agrovet Buzz, 1(6): 43-47.

Shaver, R.D. (1997). Nutritional risk factors in the etiology of left displaced abomasum in dairy cows: a review. J. Dairy Sci., 80: 2449-2453.

Shaw, J.C. (1956). Ketosis in dairy cattle. A review. J. Dairy Sci., 39: 402.

Smith, B.I. (2005). Management of periparturient disorders in dairy cattle. Vet. Food Anim., 21: 503-521.

Strang, B.D., Bertics, S.J., Grummer, R.R. and Armentano, L.E. (1998). Effect of long-chain fatty acids on triglyceride accumulation, gluconeogenesis, and ureagenesis in bovine hepatocytes. J. Dairy Sci., 81: 728-739.

Sudhan, N.A., Singh, R., Singh, M and Soodan, J.S. (2005). Studies on prevalence, etiology and diagnosis of sub clinical mastitis among cross bred cows. Indian J. Anim. Res., 39(2): 127-130.

Teli, A.S. and Ali, S.L. (2007). Economic implications of bubaline ketosis – A clinical study of effects on milk yield. Vet Scan., 2(1): 11-14.

The Hindu (2009). Date:28/12/2009. http://www.thehindu.com/2009/12/28/stories/2009122852521800.htm

United States Department of Agriculture (1996). Animal and Plant Health Inspection Service, Veterinary Services. 1996. Part 3: Reference of 1996 dairy health and management. USDA Anim. Plant Health Inspect. Serv., Vet. Serv. Ctr. Epidemiol. Anim. Health, Natl. Anim. Health Monitoring Syst. Ft. Collins, CO. Info. sheet no. N212.1196.

Upadhya, S.R., Sharma, Neelesh ans Pandey, V. (2007). Nervous ketosis in buffalo-A case report. Intas Polivet, 8(2): 404-406.

Van Saun, R.J. (1997). Nutritional profiles, A new approach for dairy herds. The Bovine Practitioner, 31: 43-49.

Van Saun, R.J. (2007). Application of a pooled sample metabolic profile for use as a herd screening tool. In: Proceedings of Danish Bovine Practitioner Seminar, Middelfart, Denmark, January 24-25, 2007. p.8.

Varga, G.A. (2004). Feeding strategies for transitioning cows into lactation. In: Proc. Of Penn State Dairy Cattle Nutrition Workshop, pp. 57-63.

Wang, C., Beede, D.K., Donovan, G.A., Archbald, L.F., DeLorenzo, M.A. and Sanchez, W.K. (1991). Effects of dietary negative cation-anion difference and high calcium content prepartum on calcium metabolism, health, lactational and reproductive performance of Holstein cows. J. Dairy Sci., 74: 275 .

Weller, R.F. and Cooper, A. (1996). Health status of dairy herds converting from conventional to organic dairy farming. Vet. Rec., 139(6): 141-142.

Woods, G.T. (1986): Practices in Veterinary Public Health and Preventive Medicine in the United States. Iowa: Iowa State University Press, USA. pp 127-130.

Zhu, L.H., Armentano, L.E., Bremmer, D.R., Grummer, R.R. and Bertics, S.J. (2000). Plasma concentration of urea, ammonia, glutamine around calving, and the relation of hepatic triglyceride, to plasma ammonia removal and blood acid-base balance. J. Dairy Sci., 83: 734-740